(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 407 943 A1**

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number: 90113100.3

(51) Int. Cl.5: A61F 13/00, A61L 15/16

(22) Date of filing: 09.07.90

(30) Priority: 11.07.89 JP 178833/89

(43) Date of publication of application: 16.01.91 Bulletin 91/03

(84) Designated Contracting States: DE FR GB

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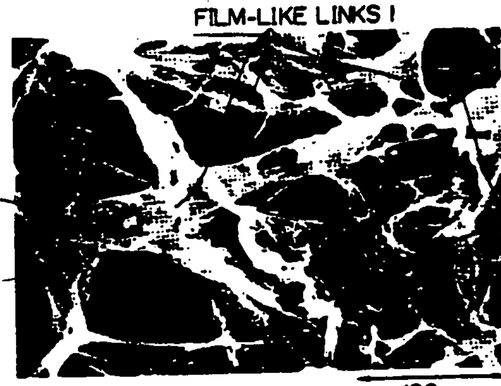
(54) **Wound dressing and method of manufacturing the same.**

(57) A wound dressing, wherein porous structure having many pores (2) is formed by a three-dimensional structure, which is composed of a combination of minute film-like links (1), in a wound dressing of said porous structure.

A method of manufacturing a wound dressing, which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring said homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispersed; and freeze-drying said dispersion gel as it is (or after warming with stirring and further being left cooled, or under the presence of a freezing state controlling agent).

Fig.2A TYPE 2 (SURFACE) DISPERSION GEL CONCENTRATION 0.2%



WOUND DRESSING AND METHOD OF MANUFACTURING THE SAME

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a wound dressing, and more particlarly to a wound dressing which is suited for treatment of wounds, for example, burn and trauma.

Description of the Prior Art

To date, various dressings have been developed to treat a broad range of skin defects due to burn, trauma or wound.

While a variety of structural contrivances have been made for such wound dressings, those being often used at present are in the form that silicone film is sticked to one side of a fabric or sponge structure to inhibit the invasion of bacteria. This structure creates primary vital adhesion by absorbing the exudate from the affected site to form fibrin, and in turn enables secondary vital adhesion by ensuring the subsequent penetration of fibroblasts and capillaries, thus resulting in the strong adhesion of the dressing to the wound surface. However, since the silicone film has body fluid proteins accumulated under the film, it has great danger of becoming a source of nourishment for growth of bacteria being present on the wound surface, so that it has a shortcoming that the healing of wound is rather disturbed.

In the sponge structure as described above, moreover, its required performances such as good contacting ability with the above-mentioned exudate and blood, the efficiency of drug release, the good dressing ability of affected sites, etc. have been examined less sufficiently to date. For example, the structure disclosed in the U. S. Patent No. 3113568 is formed as a barrier 20 which is made of foam with network structure provided under a pad 11 as illustrated in Figs. 12 and 13. Unit cells 21, which constitutes this barrier 20, present polyhedral structure having each face 22 (which is three-dimensionally linked by leg-like links 23 to become pores) formed. Therefore, this structure is simply a network thing, not structurally satisfying each of the above-mentioned required performances to a sufficient extent. In other words, since the network things are only linked by the leg-like links 23, it involves the following problems: the contact area having contacts with exudate and blood is not sufficient; the mechanical strength of the network object is small; the drug dispersed from the network things (which are contained in the structure be forehand) is released less efficiently; and the barrier effect on bacteria still remains to be improved. These problems are found generally in other known sponge structure.

OBJECTS AND SUMMARY OF THE INVENTION

Continuing various studies on wound dressings including the conventional therapeutic dressings for skin defects, the present inventor has succeeded in specifically modifying the porous structure of a sponge structure, etc., thus reaching the present invention.

The first object of the present invention is to provide a wound dressing, which can enlarge the contact area between exudate or blood and the material, promote coagulation and incrustation, increase the mechanical strength, disperse the drug on the suface of the material to raise the efficiency of its release, enhance the barrier efficiency without reducing the permeability of moisture and vapor, and obtain higher dressing effect at the stage of incrustation.

The second object of the present invention is to provide a method by which said wound dressing can be manufactured efficiently and well reproducibly.

That is to say, the present invention relates to a wound dressing, wherein porous structure having many pores is formed by a three-dimensional structure composed of a combination of minute film-like links in a wound dressing of said porous structure.

In addition, the method of manufacturing in accordance with the present invention is divided into the

following three types:

The first type of manufacturing method is a method of manufacturing a wound dressing which has the following processes: warming with stirring a base material-containing solution to produc a homog neous solution; cooling with stirring this homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispered; and freeze-drying this dispersion gel.

The second type of manufacturing method is a method of manufacturing a wound dressing which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring this homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispersed; warming with stirring this dispersion gel; and freeze-drying this warmed gel after being left cooled.

The third type of manufacturing method is a method of manufacturing a wound dressing which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring this homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispersed; and freeze-drying said dispersion gel under the presence of a freezing state controlling agent which controls the freezing state of this dispersion gel.

Other objects, features and advantages of the invention will appear more fully from the following detailed description thereof taken in connection with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figs. 1 to 11 illustrate the embodiments of the present invention, wherein:

Fig. 1A is a scanning electron micrograph of a part of the film structure of the surface of Type 1 wound dressing;

Fig. 1B is a similar scanning electron micrograph of the internal portion of said wound dressing;

Fig. 1C is a similar scanning electron micrograph of the wound surface side of said would dressing;

Fig. 1D is a scanning electron micrograph of the film structure of the whole section of said wound dressing;

Fig. 2A is a scanning electron micrograph of the film structure of a part of the surface of Type 2 wound dressing;

Fig. 2B is a similar scanning electron micrograph of the internal portion of said wound dressing;

Fig. 2C is a similar scanning electron micrograph of the wound surface side of said wound dressing:

Fig. 2D is a scanning electron micrograph of the film structure of the whole section of said wound dressing;

Fig. 3A is a scanning electron micrograph of the film structure of a part of the surface of Type 3 wound dressing;

Fig. 3B is a similar scanning electron micrograph of the internal portion of said wound dressing;

Fig. 3C is a similar scanning electron micrograph of the wound surface side of said wound dressing;

Fig. 3D is a scanning electron micrograph of the film structure of the whole section of said wound dressings;

Fig. 4 is a sectional diagonal view of a wound dressing;

Fig. 5 is a sectional view showing a state of pouring dispersion gel into a mold;

Fig. 6 is a schematic view showing the freezing state of dispersion gel used for manufacturing Type 1 wound dressing;

Fig. 7 is a schematic view showing the state of dispersion gel used for manufacturing Type 2 wound dressing;

Fig. 8 is a sectional view and a graph showing a cup used for a vapor permeability test and the test results;

Fig. 9 is a sectional view and a graph showing a device used for a serum permeability test and the test results;

Fig. 10 is a graph showing the results of a plasma permeability test;

Figs. 11 (A), (B), (C), (D) and (E) are respective plane views of a part of a wound dressing having various perforations;

Fig. 12 is a sectional vi w of a conventional wound dressing; and Fig. 13 is an enlarged diagonal view of a network structural unit of said wound dressing.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The embodiments of th present invention will be hereunder described.

Wound dressings in accordance with the embodiments described below include, for example, the following three types (Type 1, Type 2 and Type 3):

Type 1

A type obtained by freeze-drying polyamino acid dispersion gel.

Type 2

A type obtained by warming and then freeze-drying polyamino acid dispersion gel.

Type 3

A type obtained by freeze-drying polyamino acid dispersion gel containing cyclohexane.

While the manufacturing methods of these types will be described later, the structure of each type of wound dressing obtained is shown in Figs. 1 to 3, respectively. In the description below, however, the respective areas of the surface, internal portion and wound surface side of the wound dressing are as shown in the drawings. But usually, the surface represents an area (surface layer) having a thickness of 10 to 200 µm from the most external surface, the wound surface side means an area having a thickness of 10 to 200 µm from the most external surface at the opposite side of the surface, and the internal portion signifies an area (internal layer) other than the surface and the wound surface side. The section of a wound dressing in Fig. 4 illustrates a situation in which core or reinforcing material composed of nylon mesh 3 is embedded, causing the textual state to have changed with this core material as a border.

Figs. 1A, 1B and 1C are the scanning electron micrographs of the film structure of a part each of the surface, internal portion and wound surface side of Type 1 wound dressing. It can be seen from these micrographs that Type 1 wound dressing has a unique porous structure which is so constituted as to contain pores 2 through three-dimensional linkage of minute film-like links (or film pieces). This is completely different from the porous structure which is constituted by leg-like links as shown in Fig. 13. To be specific, the film-like links 1 are produced in correspondence with dispersed particles in the dispersion gel as will be described later, possessing a relatively large width, and link between pores 2 in a continuous way (as continuous pores) without being isolated. And the pores 2 themselves are large in size and numerous as well. Many of these pores are found especially in the internal port ion of the wound dressing, but there are also numerous pores in the wound surface side, and relatively tight surface layers are formed on the surface (see Fig. 1D showing a scanning electron micrograph of the film structure of the whole section.)

According to Type 1 structure, the marked effects, which have not been available to date, can be obtained.

(1) Since many pores 2 (which have a substantially uniform pore diameter in each region) are embedded in the three-dimensional structure formed by the film-like links 1, the contact area between exudate or blood from the wound surface and the material is enlarged, so that coagulation and incrustation can be promoted, and mechanical strength can be increased.

(2) In addition, the release efficiency of a drug (which can be kept contained in the material beforehand as will be described later) being present in dispersion on the surface of the material can be increased.

(3) The barrier effect can be raised without reducing moisture and vapor permeability, and more effective dressing can be obtained in the stage of incrustation.

Figs. 2A, 2B, and 2C are the scanning electron micrographs of the film structure of a part each of the surface, internal portion and wound surface side of Type 2 wound dressing, and Fig. 2D is a scanning electron micrograph of the whole section of th wound dressing. These micrographs reveal that Type 2 wound dressing, like Type 1, has a uniqu porous structure which is so constituted as to contain pores 2 through the three-dimensional linkage of minute film-like objects 1. And the structure of this Type 2 seems to be featured by a greater width of the film-like links 1 and a larger diameter of pores 2 as compared with

Type 1. This is thought to be because the freeze-drying of dispersion gel after warming, as shown in the manufacturing method which will be described later, has already changed into an intermediat state of gel between dispersion and non-dispersion gel (i.e., homogeneous gel consisting of a uniform phase with no dispersed particles) before freezing. Type 2 itself exhibits the same effects as Type 1 as well as has better strength of the dressing than Type 1.

Figs. 3A, 3B, and 3C show the scanning electron micrographs of the film structure of a part each of the surface, internal portion and wound surface of Type 3 wound dressing, and Fig. 3D shows a scanning electron micrograph of the film structure of the whole section of the wound dressing. These micrographs show that Type 3 wound dressing, like Type 1, has a unique porous structure which is so constituted as to contain pores 2 through the three-dimensional linkage of minute film-like links 1. And it seems that in the structure of this Type 3 the film-like links 1 are linked more complicatedly as compared with Types 1 and 2. This is thought to be because the presence of cyclohexane, as shown in the manufacturing method that will be described later, has made it difficult for the dispersion gel to be frozen. Type 3 has the same effects as Type 1 as well as the merits of both Types 1 and 2, and are satisfactory not only in its moisture permeability and transudation but also in its strength.

According to the dressings shown in Figs. 1D, 2D, and 3D, respectively, nylon mesh 3 has a fibrous thickness ranging from 1 to 50 denier and the number of fibers ranging from 1 to 100 per inch; for example, mesh having a thickness of 15 denier and a division number of 40 per inch is embedded, and the texture is then entangled with this mesh, thus leading to the improved strength of the dressing. And it is seen that with the mesh 3 as a border, the film texture is relatively tight on wound surface 31, having large pores 2 on surface side 30 and small pores 2 on wound surface 31. When dispersion gel 7 is poured into a mold 8 placed on a plate 42 as shown in Fig. 5, the mesh 3 serves as a filter to allow fine particles to pass from the mesh 3 to the wound surface side especially when the gel concentration is not lower than 0.2%, whereas coarse particles tend to be left closer to the surface side than the mesh 3 without passing through. As a result, as described above, the textures of both sides are varied with the mesh 3 as the border. Since the wound surface side has the pores 2 which are smaller, but more than other side of the mesh 3, its moisture permeability and strength as well as drug release are all satisfactory; and since the surface side above the mesh 3 has the pores 2 which are larger, its moisture permeability becomes still better, and its strength is also satisfactory due to the film-like links 1 having a large width and reinforcement effect added by the mesh 3, coupled with good pliability or cushiony property. In addi tion, the texture of surface 32 is relatively tight, improving the effect of preventing the invasion of bacteria from outside. Such relatively tight texture of the surface 32 is estimated to be due to the following reason: as schematically illustrated in Fig. 6, a temperature gradient showing a gradual increase in temperature from the side of the plate 42 towards the surface is formed upon freezing, and crystallites 33 of a solvent (such as benzene) are produced between dispersed particles 4 from the side of the wound surface, so that polyamino acid is pushed towards the surface, resulting in an increase in the density.

Fig. 4 is a schematic diagonal view (in which a virtual line 40 represents a living body) of the wound dressing 41 in accordance with this embodiment.

This wound dressing 41 is a film-like object, the whole of which is composed of highly biocompatible or tissue-compatible porous poly-α-amino acid and contains, for example, sulfadiazine silver as an antimicrobial agent; and it may have a thickness of 0.1 to 10 mm, for example, 1 mm, and a thin surface layer 32 having a thickness of 0.5 to 5 µm, especially 1 to 3 µm is formed on the surface. The pore diameter of the pore 2 in the surface layer 32 may be set as 20 µm or less, and the pore diameter of the pore 2 in interior 30 may range from 20 to 500 µm. There is reinforcing material composed of, for example, nylon mesh 3, embedded in the internal portion 30, increasing the strength of a wound dressing 41 to prevent it from getting torn during usage. This wound dressing 41 is also provided with many minute perforations 10 which pass through between its surface and back. The diameter of said minute perforations ranges from tens to several thousands µm, and their pitch d may be 10 mm.

Accordingly, body fluid discharged from the wound surface of the living body 40 passes through many pores 2 and infiltrates from 31 of the wound dressing 41 into the internal portion 30, as well as exudes by capillarity to the surface layer 32 through the minute perforations 10. Thus, body fluid is absorbed satisfactorily into the wound dressing 41 without remaining in the boundary between the wound surface of the living body 40 and the wound dressing 41, so that the danger of bacterial growth due to the retention of body fluid is prevented, leading to enhancement of the wound healing. The pores in the surface layer 32 are fine as described above, preventing bacterial invasion from outside.

The antimicrobial agent in th wound dressing 41 can destroy bacteria on the wound surface and thereafter inhibit infections due to bact rial invasion from outsid . This requires the antimicrobial agent to be preferably released in a trace amount at a c rtain speed. In this case, th above-mentioned base mat rial of

the porous layer is composed especially of hydrophobic poly-α-amino acid, thereby markedly limiting the circulation of the fluid in the layer and enabling the agent to be released prolongedly.

In this example, in addition, it is possibl to allow the antimicrobial agent to be contained in the porous layer and develop its tim -release effect. For this purpose the content of the antimicrobial agent may b 0 to 100 parts by weight or 0 to 50 wt% (against 100 parts for the base polymer).

Highly biocompatible or tissue-compatible poly- α -amino acids used in this example include poly γ-benzyl-L-glutamate) (PBLG) poly(L-leucine), poly(N' -carbobenzoxy-L-lysine), and the combinations of these amino acids. These poly-α-amino acids are film materials having superb workability in particular since they are hydrophobic, readily polymerized, and soluble in benzene or dioxane that can be freeze-vacuum dried.

Moreover, local antimicrobial agents useable in this example include sulfadiazine silver, sulfadiazine zinc, sulfadiazine cerium, silver nitrate, and gentamicin. These antimicrobial agents are added to the above-mentioned highly histotropic porous film materials, and wound dressings can be produced with the resulting mixtures.

Furthermore, other agents such as vasoconstrictors (for hemostasis) and analgesics can be allowed to be contained in the porous layer in combined use with the above-mentioned antimicrobial agents.

In the wound dressing in accordance with this example, the core material 3 embedded in the porous layer (that is, lying in between) plays a role of giving mechanical strength to said dressing, and dresses and protects the wound surface for a certain treatment period of, for example, deep dermal burn and deep burn, then detaching the porous layer. Upon such detachment, the base material remaining in the tissues reproduced is decomposed and absorbed in the living body. In this sense, particulary, unless the internal layer being the porous one has some thickness (0.1 to 10 mm) as described above, the portion adhering to the tissues would be detached. And the efficiency of removing the dressing after treatment can be improved by controlling the position at which the core material is embedded.

Applying the dressing to the wound surface leads to incrustation joined by exudate and blood. If the nylon mesh 3 is involved in it, the whole dressing can be removed by detaching the nylon mesh 3. This makes it necessary to properly control the position at which the nylon mesh should be incorporated.

The wound dressing in accordance with this example, when used with its attachment to the living body, preferably has the flexibility with which said wound dressing bends in correspondence with any movement of the living body; that is to say, it is readily detached from the living body if it has no flexibility. To provide the dressing with such flexibility, it is preferable that the above-mentioned core material 3 has proper flexibility (or elsticity). Core materials 3 as useable include natural fibers (such as protein fiber, cellulose fiber, and mineral fiber), synthe tic fibers (made of, for example, polyurethane, polyolefin, polyvinyl chloride, polyvinylidene chloride, polyamide, silicone, and polyester) and metallic fibers (made of, for example, stainless and copper). The core material is desirably in the form of mesh, and can be produced in nylon mesh or silicone gauze.

It is desirable that a substance having good affinity for the living body (or enhancing the wound healing) is allowed to adhere to at least one side (especially the wound surface side) of the wound dressing in accordance with this example. Provided with this substance layer laminated, the wound dressing can promote initial vital adherence and inhibit retention of the exudate between the dressing and the wound surface, thus accelerating the treatment. In the process of lamination, a porous layer of the above-mentioned substance is provided, and a dressing is then formed on this layer by the above described method, or a solution of said substance is applied to the surface of the dressing, followed by freeze-drying. The above-mentioned substances include such serum proteins as fibrinogen, albumin, γ-globulin and fibronectin, collagens (including atherocollagen), gelatin, and mucopolysaccharides.

Among these, fibrinogen is a blood coagulating protein and forms fibrin by the action of thrombin. Since fibrin exhibits highly superb adhesive and proliferative properties towards fibroblasts, application of fibrinogen to the wound surface side of the dressing causes the development of its hemostatic effect and, at the same time, reveals its good vital adhesion and therapeutic effect for the wound. In addition, since collagen is a material exhibiting excellent adhesive and proliferative properties towards fibroblasts, the dressing likewise exhibits vital adhesion and therapeutic effect for the wound.

Next, the process of manufacturing each type of wound dressing described above will be explained.

First, a mold 8 having the size of 52 cm x 14 cm as shown in Fig. 5 is used, and nylon mesh 3 having a weight of 0.26 g per cm² is extended at the level of 5 mm off the bottom inside said mold. In preparing dispersion gel 7 (polyamino acid dispersion gel) to be poured into the mold 8, the following mixture is prepared in case that, for example, the concentration of poly(L-l ucine) is 0.11 w/v%. The preparation is performed normally at a poly(L-leucin) concentration ranging from 0.01 to 1 w/v%.

Benzene	10 lit. (1 batch)
Poly(L-leucine)	11 g
Sulfadiazine silver	4 g

While being stirred, this mixture is warmed to no less than 55° C, a temperature at which the solution makes no change in structure, especially to 70 to 75° C, with benzene not evaporated, and obtained as a uniform solution for over three hours. When converted to the volume of pouring into the above-mentioned mold 8, the composition of this homogeneous solution is as follows:

Benzene	728 ml (poured into 10 mm thickness)
Poly(L-leucine)	0.8008 g
Sulfadiazine silver	0.2912 g

A useable solvent is desirably benzene, but another solvent of polyleucine can be used.

<Production of Type 1>

The homogeneous solution prepared above is cooled with stirring to a temperature range from no more than 55° C to approximately room temperature, thereby leading to preparation of the dispersion gel which is formed by the dispersion of dispersed particles with a particle size of 10 to 1000 µm containing poly (L-leucine), benzene, and sulfadiazine silver. Furthermore, after said homogeneous solution is cooled to room temperature as it is into homogeneous gel, dispersion gel can be prepared by performing the operation of mashing or filtering the homogeneous gel. With operating efficiency taken into consideration, however, it is effective to prepare the homogeneous solution by cooling it with stirring as described above. The dispersion gel obtained is composed of the gelled dispersed particles that are dispersed in a dispersion liquid (which is very trace in amount). And next, this dispersion gel is, as shown in Fig. 5, poured into the mold 8 as it remains at room temperature, and is freeze-dried further as it is. The freezing temperature is set at 0 to -40° C (e.g., - 10° C), and the subsequent drying is performed at 0 to 80° C, for example, 10° C (the temperature of the plate 42) with benzene evaporated under reduced pressure. The state upon said freezing is thought to be as follows: as schematically illustrated in Fig. 6, freezing progresses from the side of the plate 42 (wound surface); free benzene 33 between dispersed particles 4 is promptly crystallized; and the crystallization then occurs gradually from the bottom towards the top, thus followed by the formation of a fibrous structure in the wound surface side 31, a network structure in the internal portion (internal layer) 30, and a relatively tight structure in the surface 32, respectively, during the above-mentioned course. And said dispersion particles 4 represent a portion constituting the already described film-like matter 1, and many pores are formed at the space where benzene has been evaporated.

Minute perforations 10 with 1 mmø or 2 mmø are formed in zigzags at intervals of 10 mm in porous film with the above obtained nylon mesh built in, and a wound dressing of Type 1 is thus produced.

<Production of Type 2>

The dispersion gel prepared above is warmed with stirring at 56° C for no more than 10 minutes (e. g., 7.5 min.) or at 52° C for 1 to 3 hours, thereby resulting in the preparation of gel in an intermediate state between the above-mentioned dispersion gel and homogeneous gel. And this gel is, as shown in Fig. 5, poured into the mold with the stirring temperature maintained. It is then left cooled to form soft gel.

This is freeze-dried in the same manner as described above, followed by the formation of minute perforations to produce a wound dressing of Type 2. In case of this Type 2, since the dispersion gel is warmed and poured into the mold as described above, it is thought that warming has allowed the interaction of the dispersed particles 4 prior to freezing as schematically illustrated in Fig. 7, causing the production of the gel in the intermediate state and thus resulting in the formation of a unique structure as shown in Fig. 2.

<Production of Type 3>

This type of w und dressing can be produced by th following two manufacturing methods depending upon the time when cyclohexane is added:

(a) Added upon dissolution

When the above described homogeneous solution is prepared, cyclohexane is added in 0. 1 to 20%, preferably 0.5 to 10%, for example 1 %, of benzene and is stirred at 70 to 75°C for about one hour; then, it is cooled with stirring to a range from 55°C to approximately room temperature, thus resulting in preparation of the dispersion gel. This dispersion gel is poured into the mold at room temperature in the same manner as described above and, after freeze-drying, a wound dressing of Type 3 is produced with minute perforations formed.

(b) Added after dispersion

Cyclohexane is added to the dispersion gel used for Type 1 in 0. 1 to 20%, preferably 0.5 to 10%, for example, 1%, of benzene, and this dispersion gel is poured into the mold at room temperature in the same manner as described above and, after freeze-drying, a wound dressing of Type 3 is produced with minute perforations formed.

Since both wound dressings of (a) and (b) above has freeze-drying performed in the state that cyclohexane is allowed to be present (or is added) (however, cyclohexane is evaporated upon drying and does not remain in the film), cyclohexane makes it difficult for the gel as a whole to be frozen and brings it into an supercooled state. Thus, it is thought that this makes the process of freezing different from those of Type 1 and Type 2 and thus leads to the creation of a unique structure as shown in Fig. 3.

Cyclohexane is estimated to control the freezing proccess in this manner, but if a substance other than cyclohexane is mixed with benzene and has no great differences in melting and boiling points from benzene, it can be used as an additive substance which exhibits the same effects as cyclohexane; for example, dioxane and cyclooctane. As for the amount of addition, 0. 1 to 20% of benzene is appropriate, for example, 1 to 2% is desirable. If the rate is too low, then there is no additive effect, and if it is too high, the film structure obtained becomes defective.

Each test described below was performed with each of the wound dressings as produced above.

(1) Tensile strength

The measurements of tensile strength along the extention of nylon mesh are as follows:

Type 1: 0.69 kg/cm^2
type 2: 1.02 kg/cm^2

Both types revealed the strength of 0.5 kg/cm^2 or more, proving that they were satisfactory in terms of strength.

(2) Vapor permeability

Using a cup 52, as shown in Fig. 8, a wound dressing 41 (the vapor permeating portion of which is a circle with a diameter of 6 cm) is extended, and with a ring-shape portion 50 tightened and sealed by paraffin 51, water moving through the wound dressing 41 was obtained as permeating moisture from an increase in the weight of a drying agent 53 under the atmosphere of 40°C and 75% RH. The results are presented in Fig. 8.

It can be seen from these results that all of Types 1, 2, and 3 have high moisture permeability. A uniform gel freeze-dried product shown here indicates a wound dressing which was obtained by freeze-drying th above-mentioned uniform gel as it was.

(3) Serum permeability

A millipore filter holder 63, which places a wound dressing 41 at the lower end of a pipe 62 to convey equin serum 60 from a transfusion bottle 61 containing the equine s rum, was provided as shown in Fig. 9. and the flow rate of th serum dropping into a collection bottle 64 was measured while changing the height H. The results ar illustrated in Fig. 9.

These results reveal that the serum permeability of Types 1, 2, and 3 (especially Type 3) is satisfactory.

(4) Plasma permeability

For this purpose as well, with equine plasma collected in place of the equine serum 60 using the device in Fig. 9, the flow rate of it was measured in the same manner. Fig. 10 show the results.

These results also reveal that the plasma permeability of Types 2 and 3 (no test conducted with Type 3) is good.

(5) Animal experiment

Using a rabbit with a weight of about 3 kg, its dorsal region was shaved off and disinfected under general anesthesia with sodium pentobarbital, and a split-thickness skin defect having a depth of 20/1000 inch and a size of 25 x 50 mm was created with an electric dermatome. The wound surface was covered with each wound dressing, on which sterilized gauze and sterilized cut cotton were in turn placed, and was then pressed and fixed with elastic bandage. On tenth post-operative day, the wound site was macroscopically observed, and the section of the wound was then histologically observed by hematoxylin and eosin stain. When the samples of Types 1, 2 and 3, respectively, were used, the macroscopic observations revealed the completion of epithelialization in any of them, and in the histological observations these samples presented the penetration of exudate into the wound dressings as well as healthy granulation and epithelialization on the wound surface. Comparative examples such as Biobrane® by U. S. Woodroof Laboratories Inc. and OpSite® by U.K. Smith and Nephew Medical Limited being commercially available wound dressings, were tested in the same manner. As a result, macroscopic observations showed little epithelialization in both of these dressings, and in histological observations no permeation of exudate into the wound dressings was revealed in either of them, coupled with little healing confirmed on the wound surface.

It will be evident that various modifications can be made to the described embodiments without departing from the scope of the present invention.

For example, the film structure or texture of a wound dressing in accordance with the present invention can be modified in various ways depending upon the size and distribution of the above described film-like objects, the size and distribution of pores, etc. In addition, the material, composition and other aspects of the dressing do not have to be limited to those stated above. The type and amount of a solvent to be used and the location of nylon mesh may be altered, and core material may be formed with a material other than nylon mesh. Nylon mesh can be omitted. As shown in Fig. 11, in addition, minute perforations 10 to be formed in a wound dressing can also be varied into small round shape (Fig. 11 (A)), slit-like cut 10′ penetrating from surface to back as in Fig. 11 (B), cross-shaped cut 10′ penetrating from surface to back as in Fig. 11 (C), X-shaped cut 10′ penetrating from surface to back as in Fig. 11 (D), and tiny pinhole-shaped through-holes 10′ as in Fig. 11 (E). Those minute perforations shown in Fig. 11 (B) to (E) produce no cut-off residue when cuts or holes are formed, and in those shown in Fig. 11 (C) and (D) the state of the wound surface inside the dressing can be visually grasped when the intersection of cross or X letter is turned up with fingers.

In regard to the above described manufacturing methods, moreover, the above-mentioned time of cyclohexane addition may be altered in the manufacturing process of, for example, Type 3 and as occasion demands, for example, it may be added upon preparation of homogeneous gel and disperson gel, respectively.

In accordance with the present invention, as described above, since pores are contained in a three-dimensional structure made by minute film-like links, the contact area between the exudate and blood from the wound surface and the material is enlarged, thus enabling the acceleration of coagulation and incrustation as well as increasing th mechanic strength. Moreover, the release efficiency of a drug being present in dispersion on th surface of material can be raised, and the barrier effect can b increased without reducing the permeability of moisture and vapor, so that higher dressing effect can be obtained at

the stage that crust has been formed.

Claims

1. A wound dressing of porous structure having many pores wherein said porous structure is formed by a three-dimensional structure composed of a combination of minute film-like links (1).

2. A wound dressing as in claim 1, wherein said film-like links are relatively large in width and link said pores (2) continuously (as continuous pores) without isolating from one pore to another, and said pores are large in size and number as well and are present numerously in the internal portion and the wound surface side of the wound dressing, coupled with a relatively tight surface layer formed on the surface.

3. A wound dressing as in claim 1, the whole of which is composed of a texture of porous poly-α-amino acid.

4. A wound dressing as in claim 3, in which an antimicrobial agent is contained.

5. A wound dressing as in claim 2, wherein its total thickness ranges from 0.1 to 10 mm, the thickness of said surface layer from 0. 5 to 5μ m, and the pore diameter of said pores from 20 to 500 μm (however, 20 μm or less in case of said surface layer).

6. A wound dressing as in claim 1, wherein mesh-like reinforcing material (3) is embedded and the texture of the dressing is entangled with said reinforcing material.

7. A wound dressing as in claim 6, wherein with said reinforcing material as a border, pores are large in the surface side (30) and small in the wound surface side (31) with the film texture being relatively tight.

8. A wound dressing as in claim 1, wherein minute perforations (10) penetrating between the surface (32) and the wound surface (31) are provided in a good number.

9. A method of manufacturing a wound dressing, which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring said homogeneous solution to produce dispersion gel in which the base material-containing gel particles are dispersed; and freeze-drying said dispersion gel.

10. A manufacturing method as in claim 9, wherein a mixture solution containing a solvent and poly-α-amino acid is warmed with stirring to a temperature at which said mixturre solution makes no structural change, with said solvent not evaporated, to produce a homogeneous solution, and next, said homogeneous solution is cooled with stirring to create dispersion gel (7) in which dispersed particles with a particle size of 10 to 1000 μm are dispersed, and said dispersion gel is poured into a mold (8) and frozen at 0 to -40°C and then dried at 0 to 80°C with said solvent evaporated under reduced pressure.

11. A method of manufacturing a wound dressing, which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring said homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispersed: warming with stirring said dispersion gel; and freeze-drying said warmed gel after being left cooled.

12. A manufacturing method as in claim 1 1, wherein a mixture solution containing a solvent and poly-α-amino acid is warmed with stirring to a temperature at which said mixture solution makes no structural change, with said solvent not evaporated, to produce a homogeneous solution, and next, said homogeneous solution is cooled with stirring to create dispersion gel (7) in which dispersed particles with a particle size of 10 to 1000 μm are dispersed, and said dispersion gel is warmed with stirring, poured into a mold (8) with the stirring temperature maintained, and left cooled, and then frozen at 0 to -40° C and dried at 0 to 80°C with said solvent evaporated under reduced pressure.

13. A method of manufacturing a wound dressing, which has the following processes: warming with stirring a base material-containing solution to produce a homogeneous solution; cooling with stirring said homogeneous solution to create dispersion gel in which the base material-containing gel particles are dispersed; and freeze-drying said dispersion gel under the presence of a freezing state controlling agent which controls the freezing state of said dispersion gel.

14. A manufacturing method as in claim 13, wherein said freezing state controlling agent is added in 0.1 to 20% of a solvent when said homogeneous solution is prepared.

15. A manufacturing method as in claim 13, wherein said freezing state controlling agent is added to said dispersion gel in 0.1 to 20% of a solvent.

16. A manufacturing method as in claim 13, wherein said freezing state controlling agent is mixed with a solvent and has no greatly different melting and boiling points from those of said solvent.

17. A manufacturing method as in claim 13, wherein a mixture solution containing a solvent and poly-α-amino acid is warmed with stirring to a temperature at which said mixture solution makes no structural change, with said solvent not evaporated, to produce a homogeneous solution, and n xt, said homogeneous

solution is cooled with stirring to create dispersion gel (7) in which dispersed particles with a particl size of 10 to 1000 µm are dispersed. and said dispersion gel is poured into a mold (8) under the presence of said freezing state controlling agent and frozen at 0 to -40 °C and then dried at 0 to 80 °C with said solvent evaporated under reduced pressure.

Fig. 1A

TYPE 1
(SURFACE)
DISPERSION GEL CONCENTRATION 0.1%

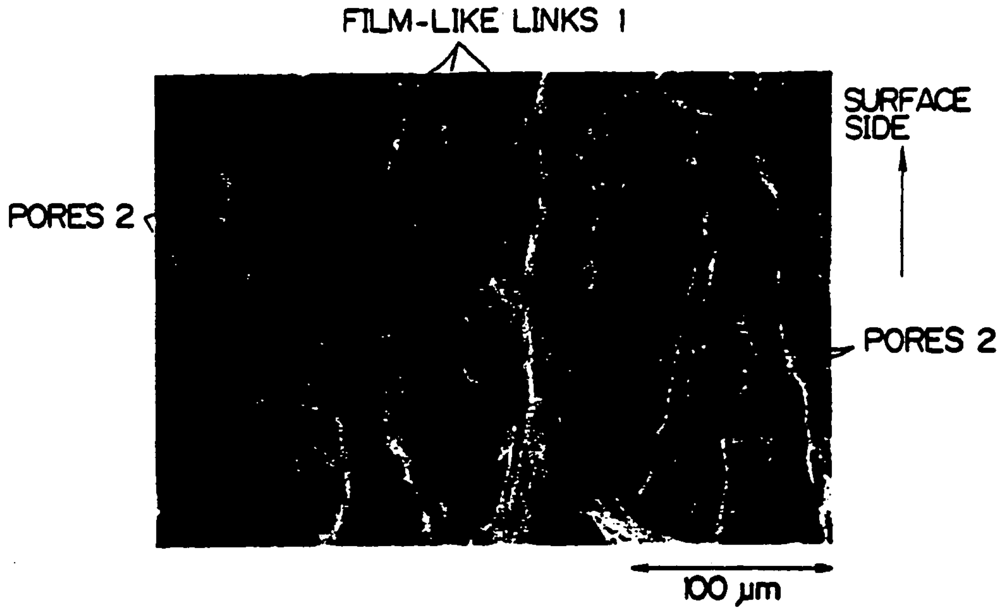


Fig. 1B

TYPE 1
(INTERNAL PORTION)
DISPERSION GEL CONCENTRATION 0.1%

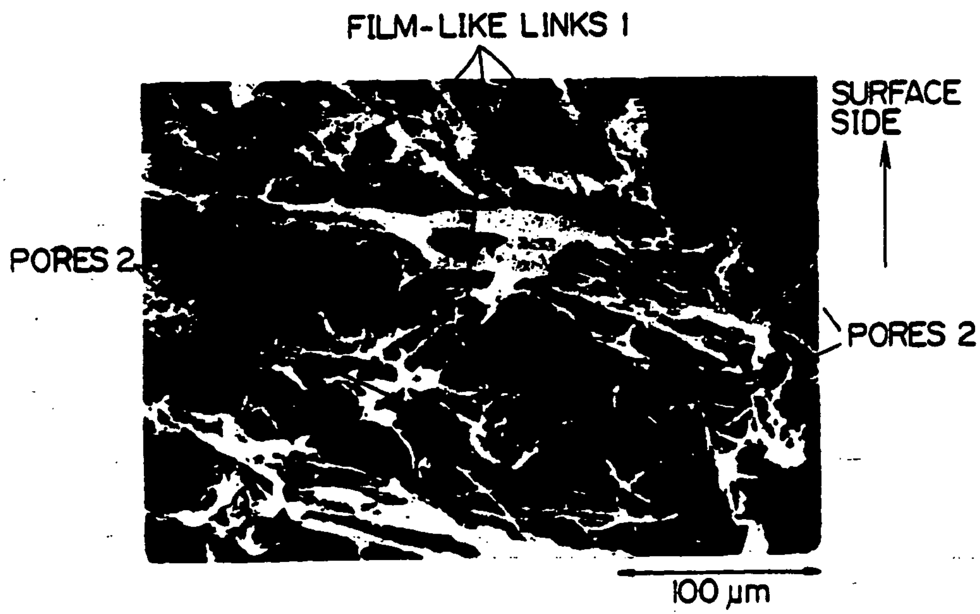


Fig.1C

TYPE I
(WOUND SURFACE SIDE)
DISPERSION GEL CONCENTRATION 0.1%

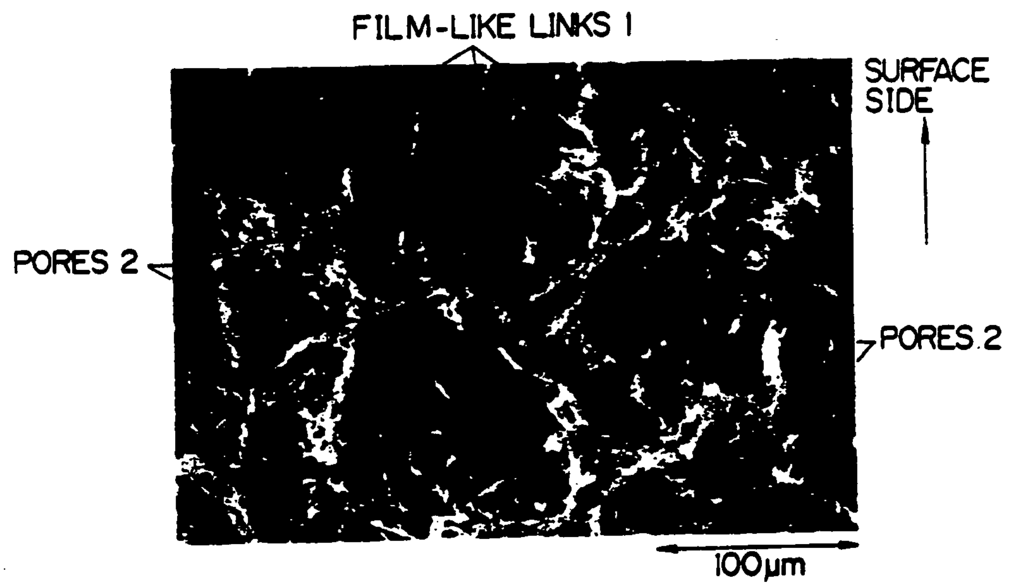


Fig.1D

TYPE I
(CROSS-SECTION)
DISPERSION GEL CONCENTRATION 0.1%

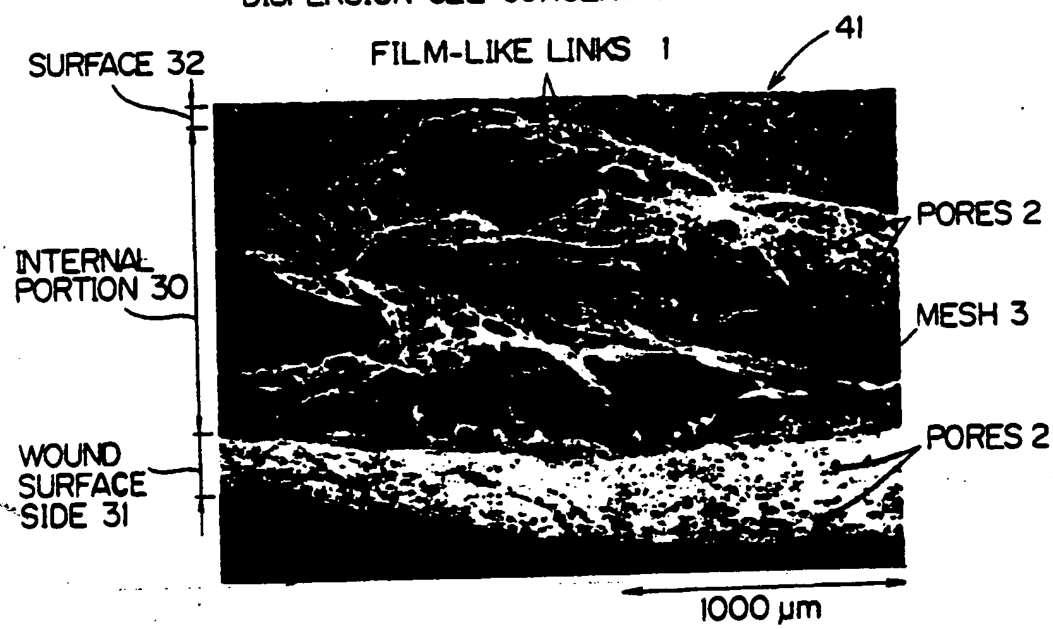


Fig.2A

TYPE 2
(SURFACE)
DISPERSION GEL CONCENTRATION 0.2%

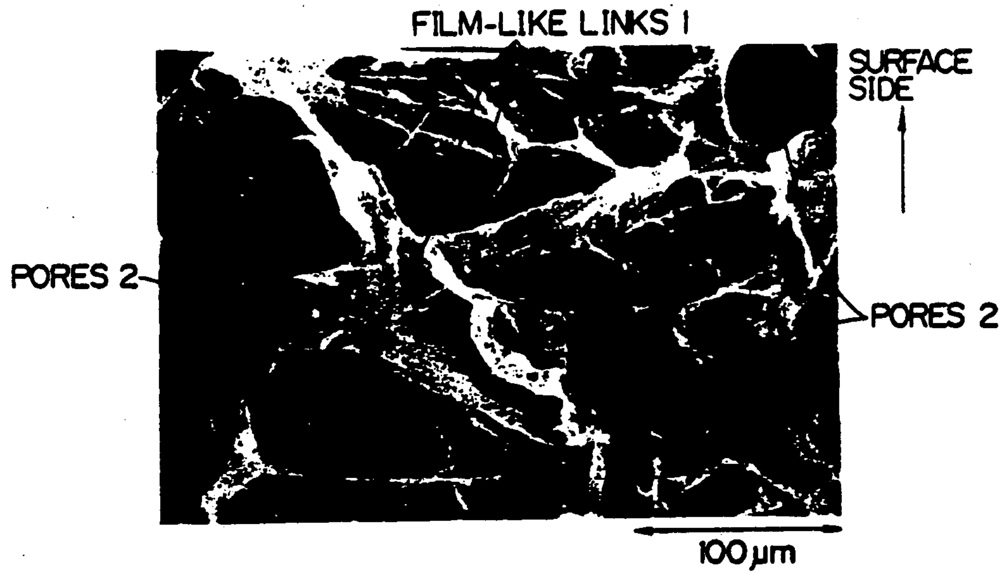


Fig.2B

TYPE 2
(INTERNAL PORTION)
DISPERSION GEL CONCENTRATION 0.2%

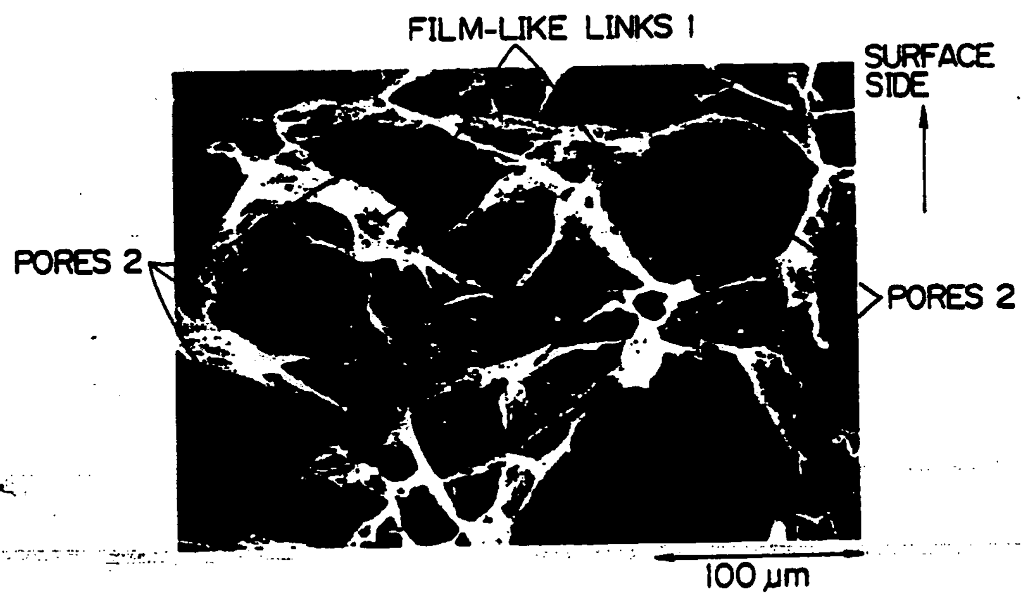


Fig.2C

TYPE 2
(WOUND SURFACE SIDE)
DISPERSION GEL CONCENTRATION 0.2 %

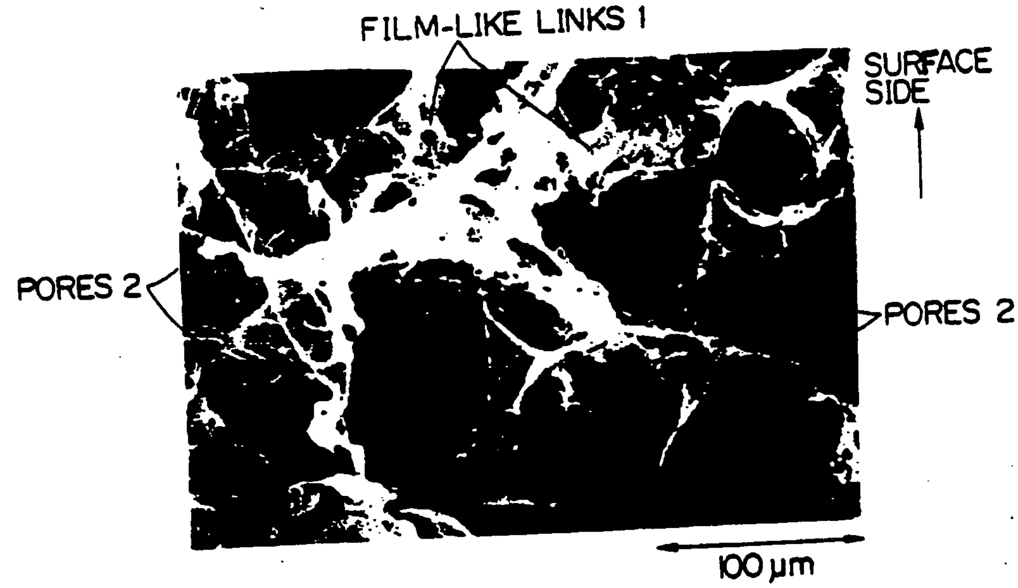


Fig.2D

TYPE 2
(CROSS-SECTION)
DISPERSION GEL CONCENTRATION 0.2 %

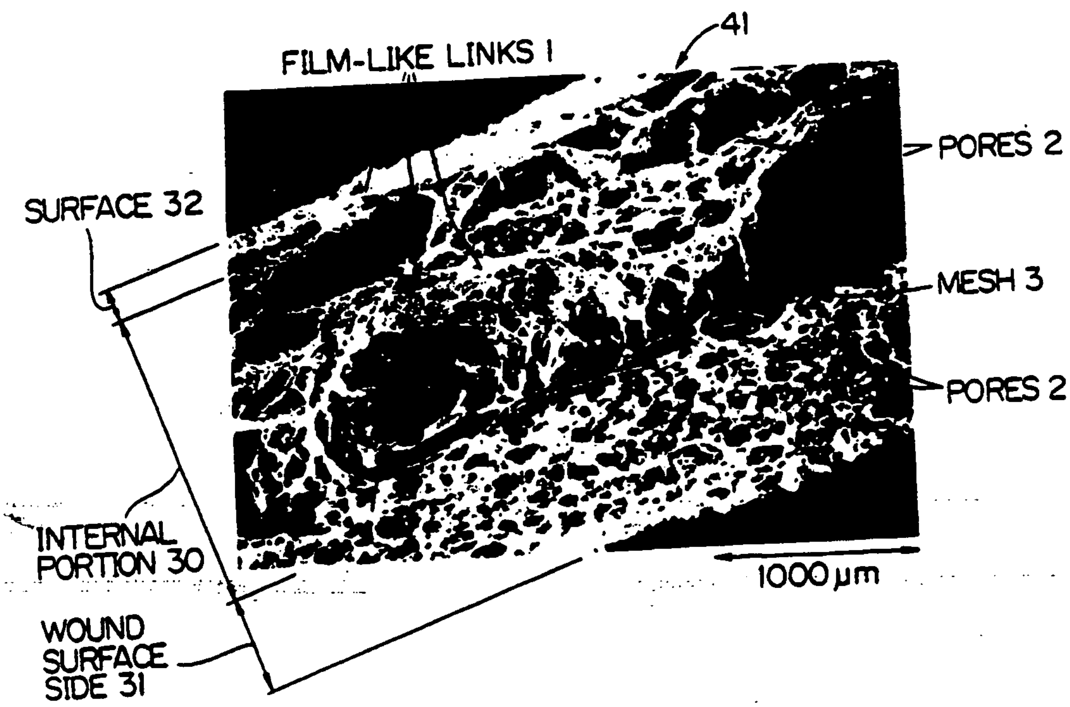


Fig. 3A

TYPE 3
(SURFACE)
DISPERSION GEL CONCENTRATION 0.2 %

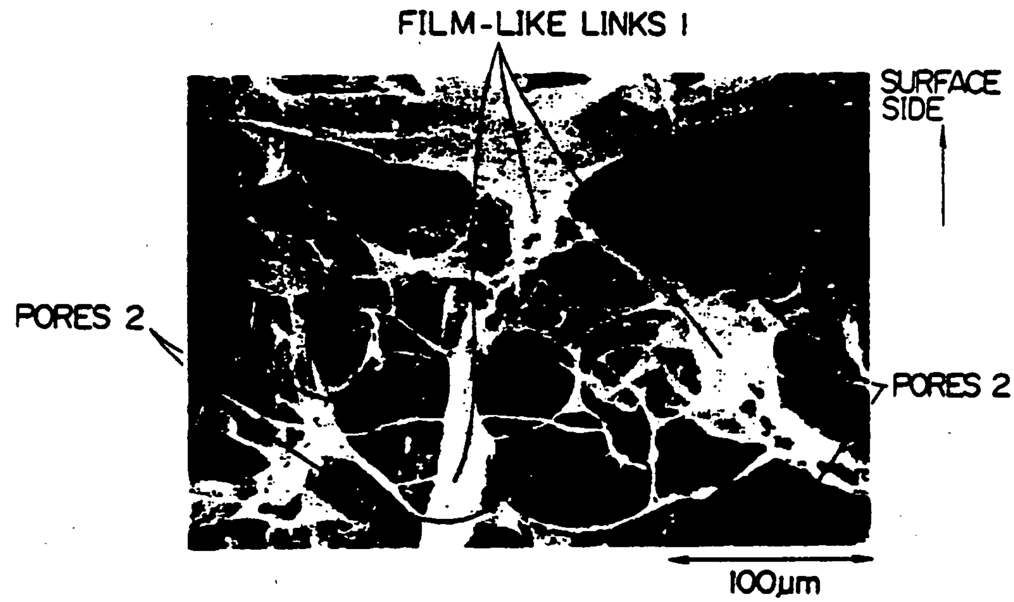


Fig. 3B

TYPE 3
(INTERNAL PORTION)
DISPERSION GEL CONCENTRATION 0.2 %

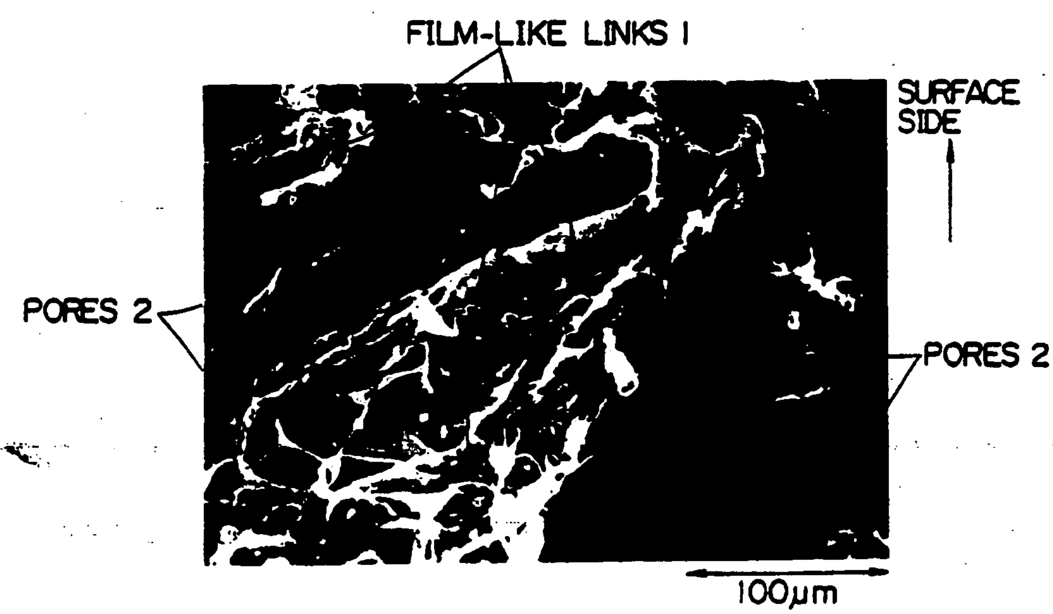


Fig.3C TYPE 3 (WOUND SURFACE SIDE) DISPERSION GEL CONCENTRATION 0.2 %

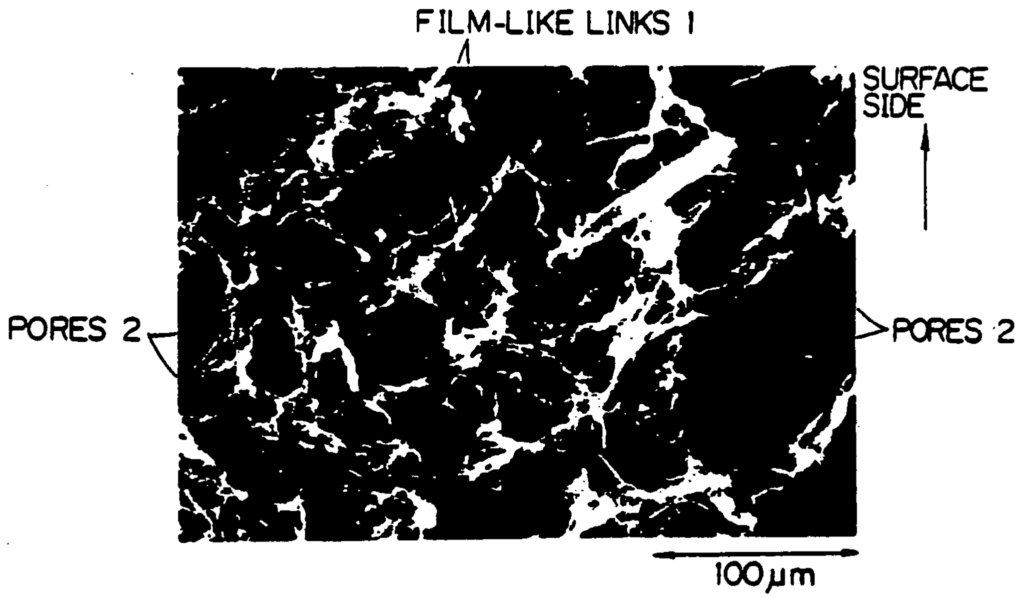


Fig.3D TYPE 3 (CROSS-SECTION) DISPERSION GEL CONCENTRATION 0.2 %

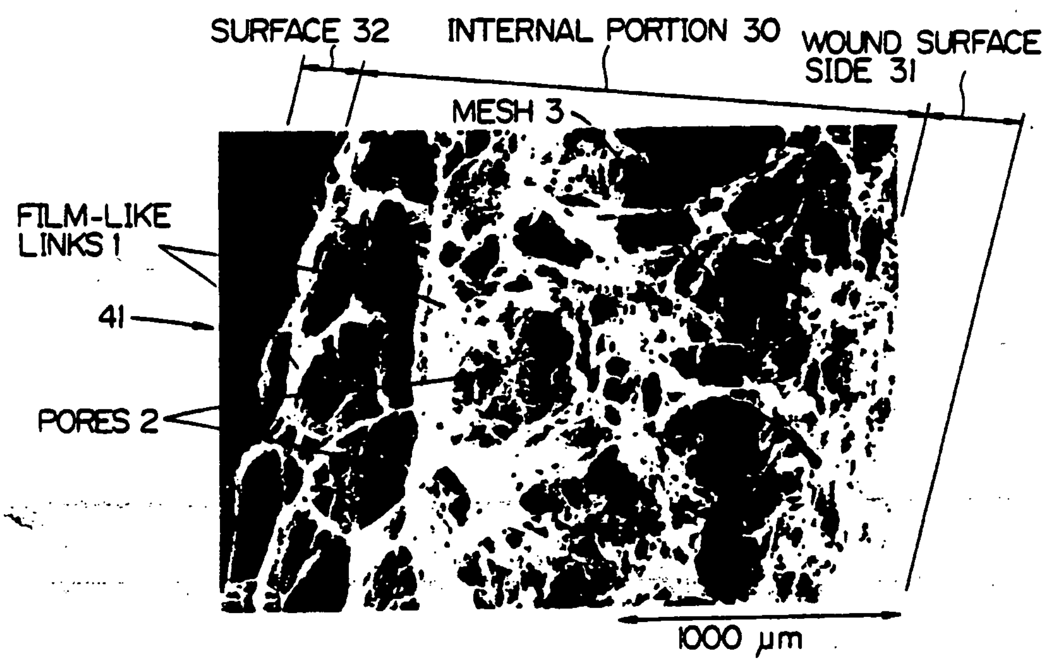


Fig.4

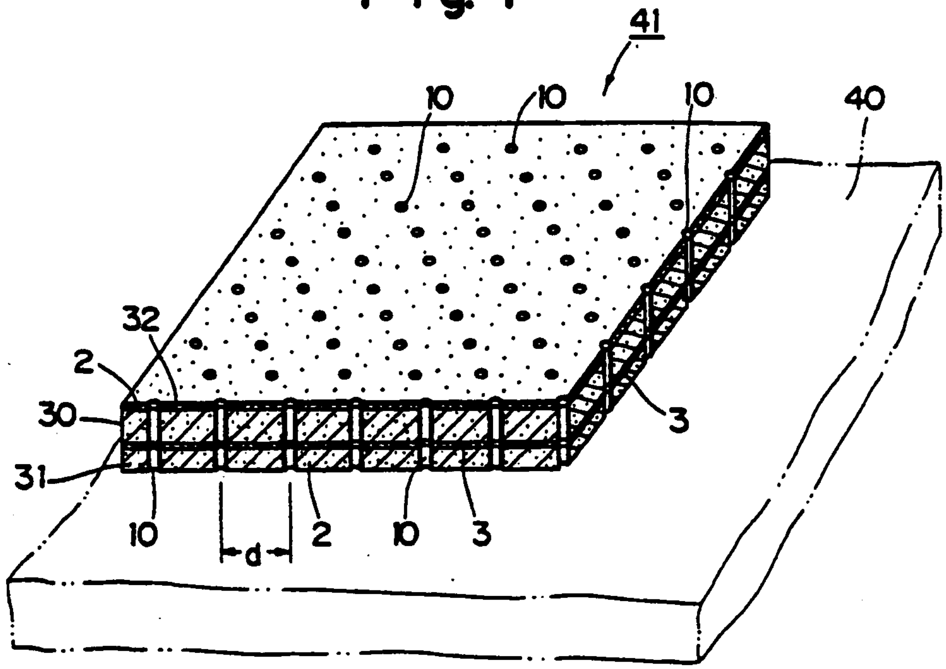
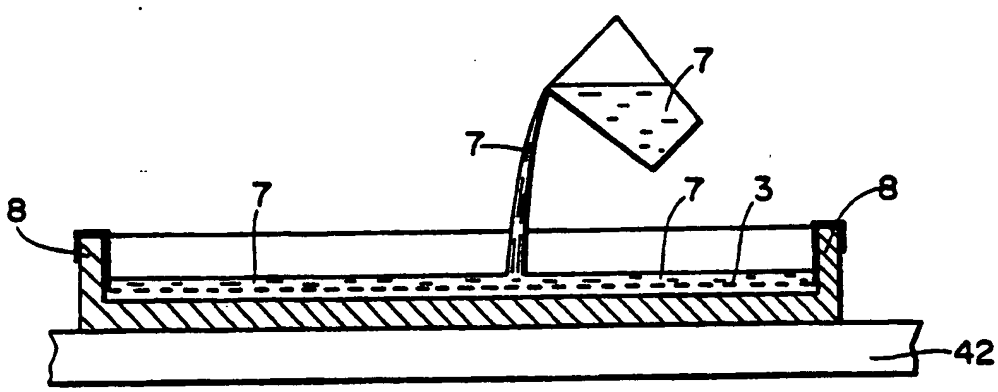


Fig.5



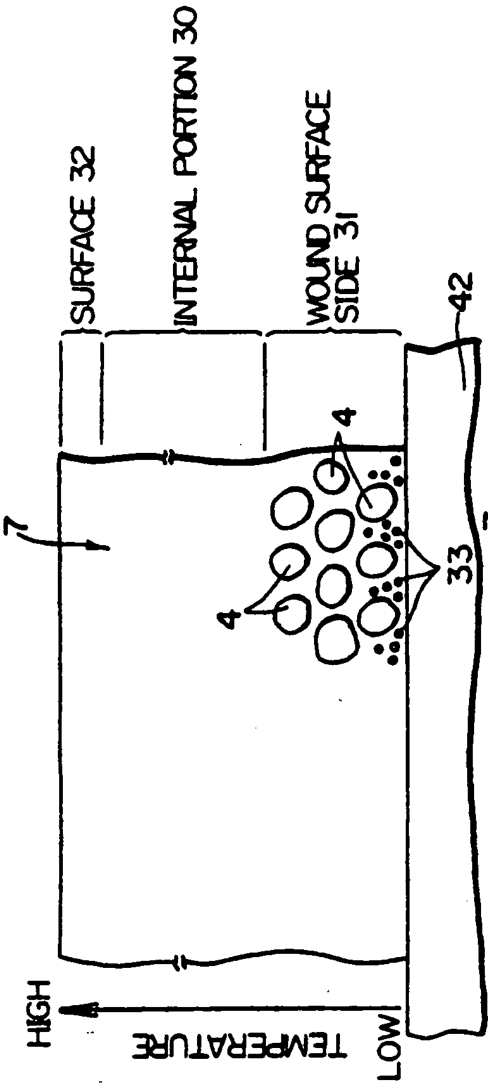

SURFACE 32
INTERNAL PORTION 30
WOUND SURFACE SIDE 31
42
7
4
4
33
HIGH
TEMPERATURE
LOW

Fig.6

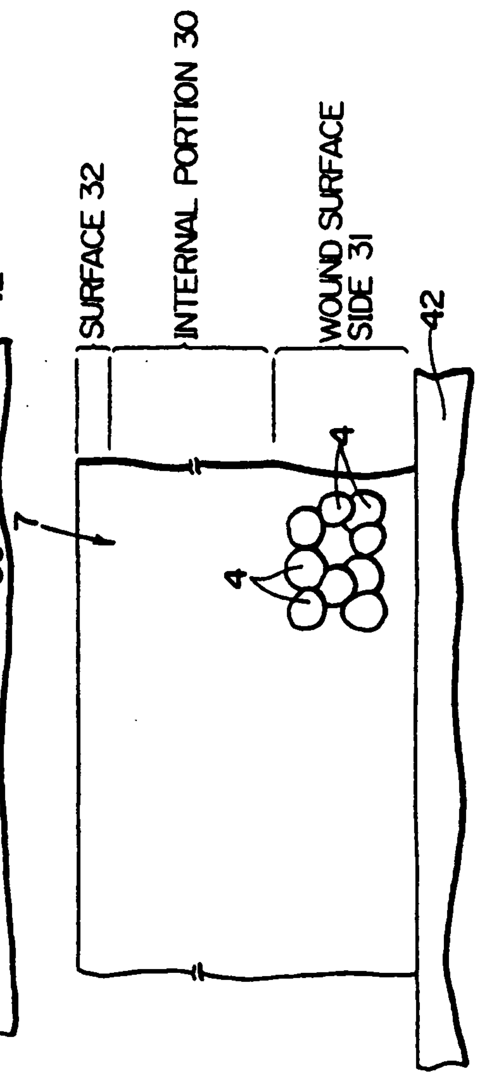

SURFACE 32
INTERNAL PORTION 30
WOUND SURFACE SIDE 31
42
7
4
4

Fig.7

Fig.8

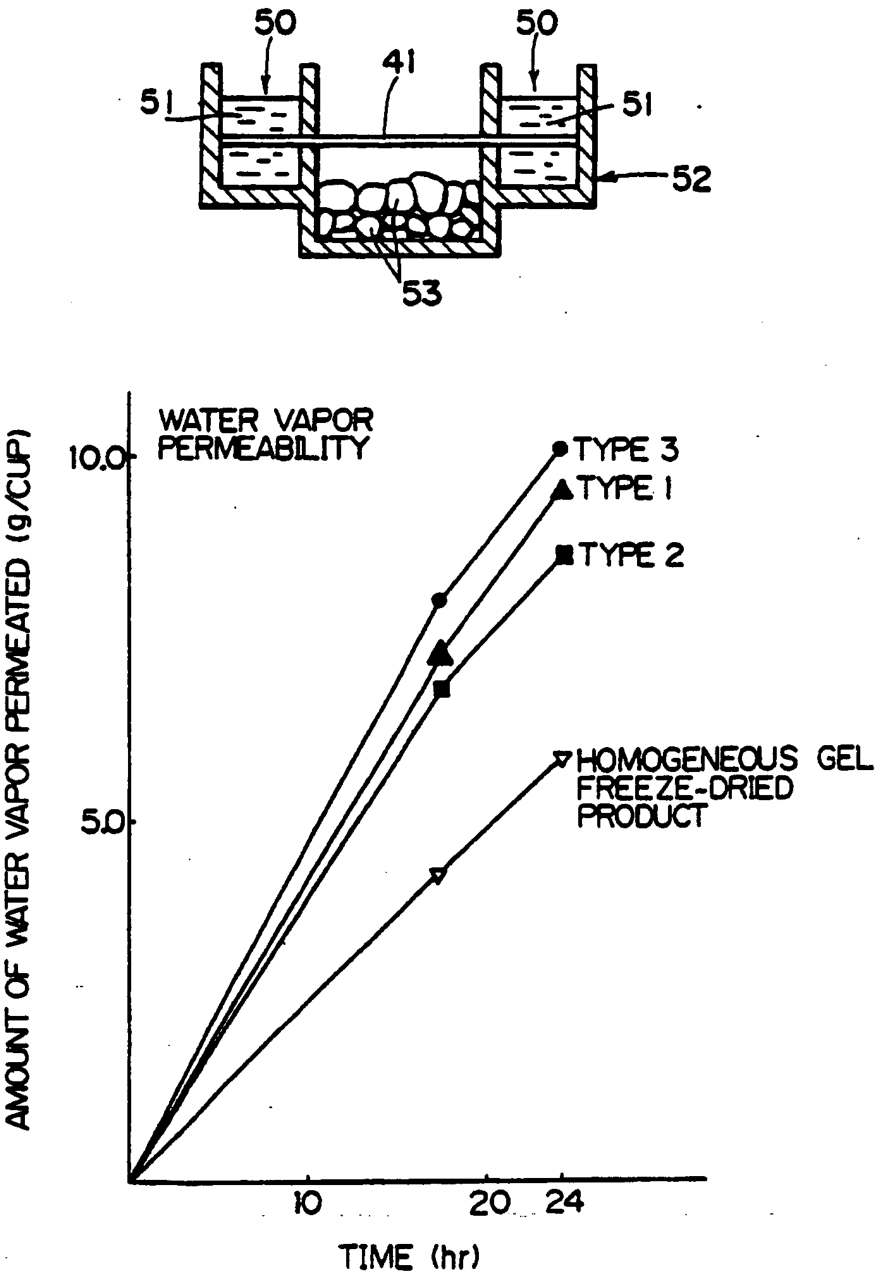

50
50
41
51
51
52
53
WATER VAPOR PERMEABILITY
AMOUNT OF WATER VAPOR PERMEATED (g/CUP)
10.0
5.0
TYPE 3
TYPE 1
TYPE 2
HOMOGENEOUS GEL FREEZE-DRIED PRODUCT
10
20
24
TIME (hr)

Fig.9

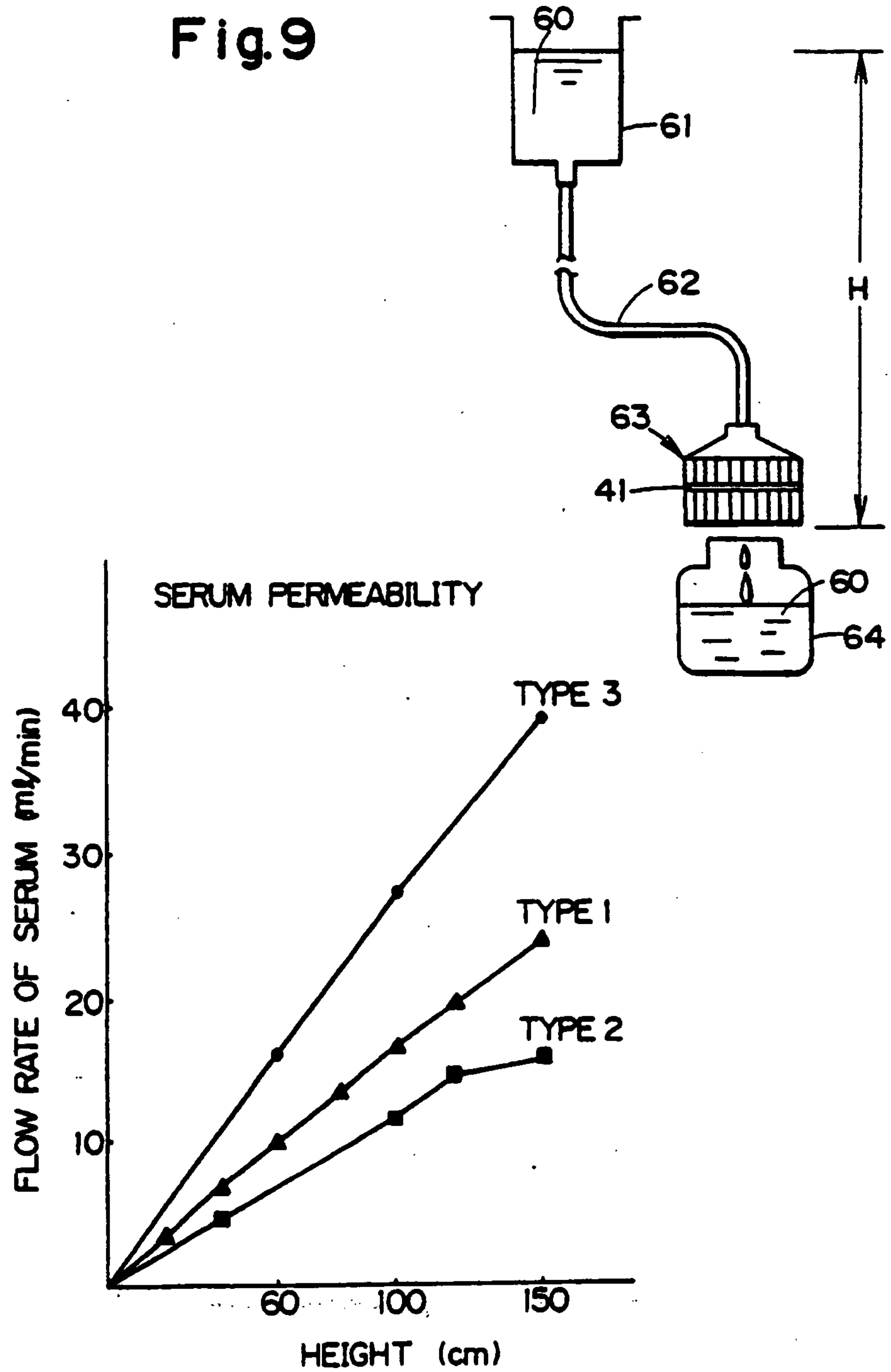

60
61
62
H
63
41
60
64
SERUM PERMEABILITY
FLOW RATE OF SERUM (ml/min)
40
30
20
10
TYPE 3
TYPE 1
TYPE 2
60
100
150
HEIGHT (cm)

Fig.10

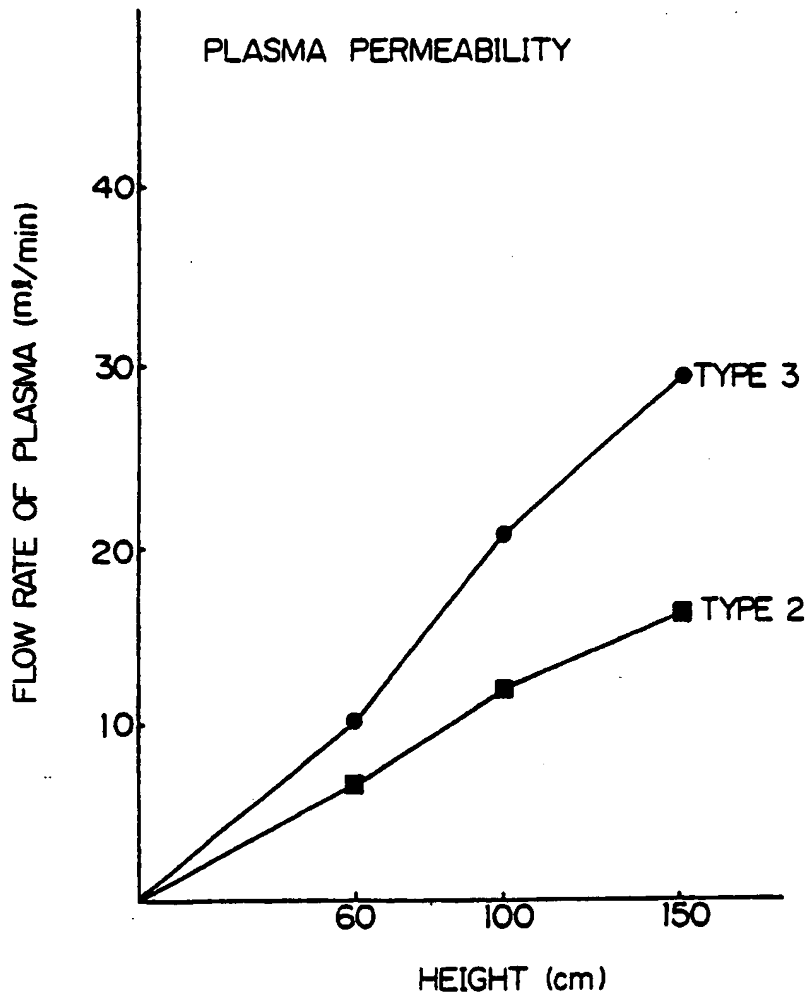

PLASMA PERMEABILITY
FLOW RATE OF PLASMA (ml/min)
40
30
20
10
TYPE 3
TYPE 2
60
100
150
HEIGHT (cm)

Fig.11

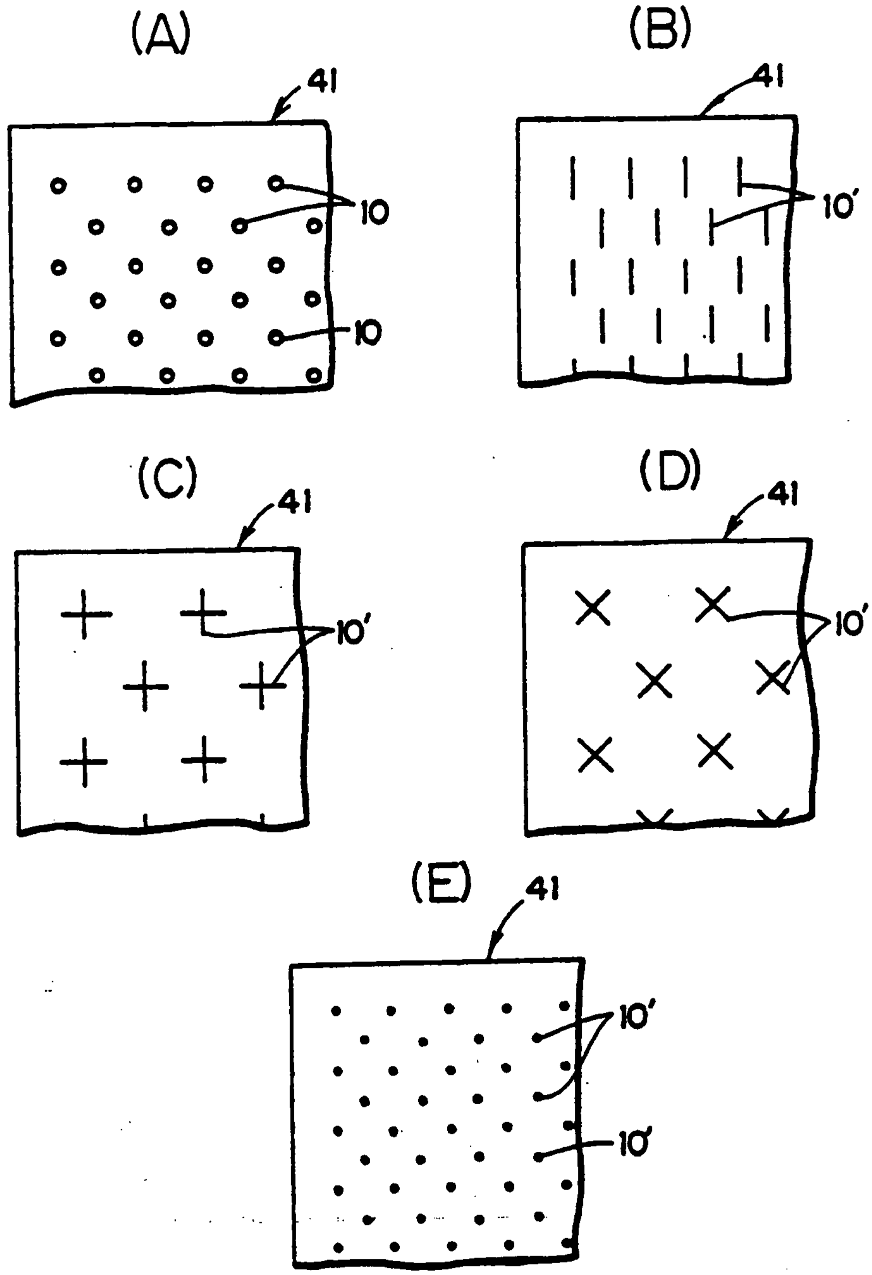


Fig.12

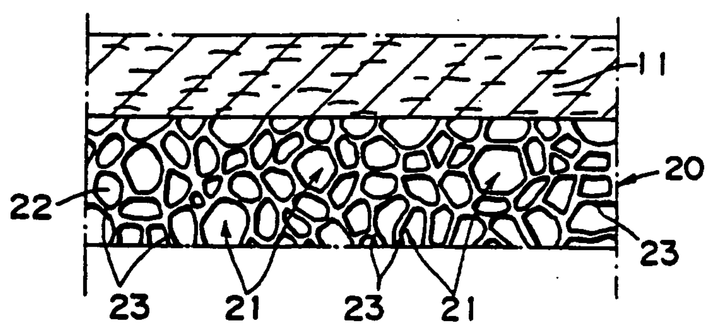
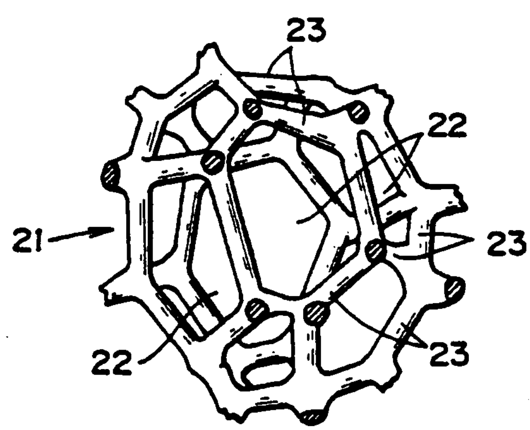


Fig.13



European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 11 3100

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 265 906 (NIPPON ZEON CO., LTD) * The whole document * ---	1-17	A 61 F 13/00 A 61 L 15/16
X	JP-A-63 115 566 (NIPPON ZEON CO., LTD) * Abstract *	1-8	
Y	---	9-17	
Y	EP-A-0 167 828 (KOKEN CO. LTD) * Page 7, lines 8-20 * ---	9-17	
X	JP-A-63 115 565 (NIPPON ZEON CO. LTD) * Abstract * -----	1-8	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 F

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	19-10-1990	ARGENTINI A.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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